

## **REMARKS**

Claims 31-40 are under examination and have been rejected. Claims 31, 32 and 35 have been amended.

### **Rejection Under 35 U.S.C. 103(a)**

Claims 31-40 stand rejected under 35 U.S.C. 103 as being unpatentable over Prince et al (U.S. Pat. No. 5,290,540) and Johnson et al (U.S. Pat. No. 5,824,307) in view of Bulow et al. and Smyth et al.

Previously, the Examiner had argued that Prince et al (the '540 patent) teaches use of a combination of an anti-viral antibody and an anti-inflammatory agent to treat RSV but not systemic administration. (See office action of 10 August 2005, at page 3, bottom paragraph over to top of page 4) but that Johnson et al (the '307 patent) teaches this.

Applicant contends that these references, when combined, fail to teach the claimed invention. Systemic administration of both antibody and anti-inflammatory agent is not taught by the cited patents in combination.

Applicants had previously directed the Examiner's attention to the reported ineffectiveness of systemically administered prednisolone in infant RSV (Bulow et al).

In response, the Examiner contends that Bulow et al. does not teach away from the claimed invention but "that steroids were not effective as a adjunct to conventional RSV therapies (page 3, column 2, top). Also, the teachings do not indicate that there was an adverse effect, but that the use of the steroid did not result in an improvement of the conventional therapy outcome." (See current office action at page 3, last 4 lines).

Applicant responds that, because the claims are directed to systemic use of combinations of antibody and anti-inflammatory agents any reference teaching that steroids were not an effective adjunct to conventional therapy does teach away from Applicant's invention, i.e., it frustrates any motivation to administer the steroid systemically, whether alone or in combination.

In sum, the Examiner fails to explain why, based on the cited art showing no improvement, there would be any motivation to combine the cited references. The Examiner's only argument appears to be that it was known that antibodies can treat RSV infection and that RSV is accompanied by inflammation (citing Smyth et al), which can be treated by steroid and therefore it would be obvious to combine them. In effect, the Examiner is treating the claimed invention as separate components, each supposedly obvious by itself, with no recognition of the combination of the two or the value of systemic administration of both. The claim must be treated as a whole when evaluating obviousness. [see *General Foods Corp. v. Studiengesellschaft Kohle*, 23 USPQ 2d. 1839, at 1840 (Fed. Cir. 1992) – "...each claim is an *entity* which must be considered *as a whole*." [emphasis in original]]

In addition, the Examiner contends that the art does not teach an adverse effect of the steroid but an adverse effect is not what is required to teach away from the claimed invention. Applicant's claims are drawn to use of a combination of antibody and steroid as the therapy regimen and the references must provide a motive to combine these components and not just the absence of any adverse effect of one of the components on the treatment regimen. For example, aspirin may not induce any adverse effect but that does not motivate its administration with antibodies.

The Examiner's contention that the teachings of the art indicate "use of the steroid did not result in an improvement of conventional therapy" (see above) is tantamount to saying that there is no motivation to combine. To establish a prima facie case of obviousness based on a combination of elements disclosed in the art the

Examiner must explain the reasons one of ordinary skill in the art would have been motivated to select the references and to combine them to render the claimed invention obvious.

In sum, if Bulow et al, as the Examiner contends, teaches that steroids are not an effective adjunct and result in no improvement of conventional therapy then it does teach away from the claimed invention.

The Examiner also relies on the '540 patent as teaching combination of antiviral and anti-inflammatory agents (citing col 4, lines 60-65) but Applicants direct the Examiner's attention to line 59 where it notes such administration is topical. Coupled with Bulow et al. there is clearly no motivation to administer steroids systemically at all (whether in combination or not).

However, while the art provides no motive to combine antibodies and steroids, the application does – by way of example.

Figure 1 of the application shows the results of a comparison of antibody alone versus the combined regimen of antibody and steroid. Each day (days 4, 6, 8, 10, 12 and 14) shows an improvement over use of the antibody alone. The Examiner contends that the art teaches no improvement so that Applicant's results are at once contrary to the art and a novel and unobvious treatment regimen. The art teaches away from Applicant's claimed combination because, if for no other reason (which Applicant does not concede), it finds no improvement.

The results of Figure 2B of the application lead to a similar conclusion (compare numbers 3, 4 and 7 for antibody alone vs. steroid alone vs. the combination, respectively). Here, a definite improvement on day 6 results for the combination. In the same way, numbers 3, 4 and 7 show the same trend for the indicated RSV infection (peribronchitis (Fig. 2C), alveolitis (Fig. 2D) and interstitial pneumonitis (Fig. 2E)).

Likewise, Figure 3B and page 25, lines 12-19 of the application shows and discusses the results of treatment with combinations of antibody and steroid. In particular, the results show an accelerated viral clearance with antibody alone, but a smaller effect on pulmonary inflammation by antibody alone (compare regimens #2 and #3 of the figure) while use of steroid alone (#4 at 16 mg/kg) shows only moderate effects on pulmonary inflammation. Conversely, use of the antibody with steroid (16 mg/kg) shows marked results (regimen #7 of the figure). Similar results are exhibited in Table 1 of Example 5.

Clearly, Applicant's results are not in concert with the contention that antibody treats virus and steroid treats inflammation and that combining the two creates no new effect. Applicant's results show an improvement using combination over antibody or steroid alone.

Further, Smyth et al still does not support the systemic treatment contraindicated by Bulow et al. For example, Smyth et al. find no correlation between severity of infection and the concentrations of any inflammatory mediators (see Abstract, lines 7-10 from the bottom) so that there is still no motivation to administer steroid systemically as opposed to topically or even to support the idea that steroid would lessen severity of infection if administered systemically.

In view of the foregoing remarks and amendment, Applicants believe that the grounds of rejection have been overcome and respectfully request that the Examiner reconsider the pending claims.

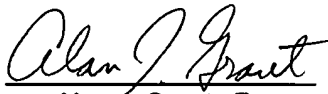
If any additional fee is due in filing this amendment, the Commissioner is authorized to charge any and all such fees to Deposit Account No. 03-0678.

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